Postdoctoral position available to develop engineered nanobodies targeting bacterial core divisome complex.

Project

Bacterial cell division is a temporally and spatially regulated process coordinated by a multi-protein complex called the divisome. The assembly of the divisome is initiated and organized by a highly conserved bacterial protein, the bacterial tubulin homologue FtsZ, which polymerizes to form a dynamic ring structure (Z-ring) that marks the site of cell division. Following ring assembly, FtsZ recruits structural and accessory proteins in an ordered manner to form the functional cell division machinery and to build a new cell wall. The precise molecular mechanisms by which the assembly and regulation of the bacterial cell division machinery is achieved remains elusive. While genetic and biochemical techniques have identified many interactions amongst cell division proteins, the overall structure and dynamics of the divisome as a (large) multi-protein complex are still completely unknown. This is particularly true in Corynebacteriales, a group including important human pathogens such as *Mycobacterium tuberculosis*, *Mycobacterium leprae* and *Corynebacterium diphtheriae*.

The aim of the project is to provide an in-depth understanding of the Corynebacteriales core divisome architecture and function, using *Corynebacterium glutamicum* as a model organism. The major objective is to understand how protein-protein interactions within the divisome link the intracellular status of the cell to the extracellular cell wall machinery, via transmembrane interactions during bacterial cell division. To overcome the challenges intrinsic to structure determination of potentially flexible transmembrane (multi-)protein complexes we will develop tools aiming at stabilizing favored conformations of these complexes in solution.

To accomplish the central objective of this project, we will produce nanobodies targeting the membrane complexes for cryo-EM and X-ray structure determination. The specific binding of the different nanobodies to the target protein complexes will be analyzed by ELISA and by immunofluorescence with fixed cells. The most promising nanobodies will be engineered to obtain larger fusion constructs, or Megabodies to aid structure determination by cryo-EM.

The project will be performed in the framework of an ANR research program and will be conducted in collaboration with the groups of Anne-Marie Wehenkel (Institut Pasteur), Ahmed Haouz (Institut Pasteur) and Mohammed Terrak (University of Liege, Belgium).

Host Institute

The successful candidate will work mainly in the group of Pierre Lafaye at Institut Pasteur for nanobodies design, engineering and production. He/she will collaborate with the group of Anne-Marie Wehenkel for the characterization of nanobodies for conformational stability or effect on enzymatic activities. He/she will have also access of the many facilities of biophysics of the institute to further characterize the nanobodies. The Institut Pasteur is a word-class research institute located downtown in Paris nearby exciting culture and city life.

Requirements

We are looking for a motivated individual with a Ph.D. degree in biochemistry or biophysics. Experience in biochemistry is essential; experience with nanobody engineering and phage display would be a plus but is not mandatory. Applicants will have to be autonomous and take initiatives.

Terms of employment

The position is for 18 months and will be filled as soon as possible. The salary will follow the Institut Pasteur guidelines.

How to apply

Interested applicants should send their CV, a cover letter describing their motivation and contact details of two academic references to pierre.lafaye@pasteur.fr.